

April 6, 2004.” Otherwise, the priority claim is accurate and recites that the instant application is a continuation of U.S. Patent Application No. 09/948,374, which application claims the benefit under 35 U.S.C. §119(e) of United States Provisional Application Serial No. 60/286,254, filed April 24, 2001 and is a continuation-in-part of United States Patent Application Serial No. 09/760,328, *etc.* That is, the priority claim is to U.S. Application No. 09/948,374 – it is the ‘374 application (“which application”) that claims the benefit of the filing of Provisional Application No. 60/286,254 “and is” a continuation-in-part of U.S. Application 09/760,328. Thus, the priority claim as recited is correct and accurate.

Accordingly, Applicants submit that this objection has been obviated and request that it be withdrawn. /

OBJECTION TO ABSTRACT

In the Office Action, the Abstract of the disclosure was objected to as insufficiently detailed. As set forth above, Applicants have replaced the original Abstract with a more detailed Abstract. Accordingly, Applicants submit that this objection has been obviated and request that it be withdrawn.

REJECTION UNDER 35 U.S.C. §112, SECOND PARAGRAPH

In the Office Action, claims 15-17 were rejected under 35 U.S.C. §112, second paragraph, as indefinite. Specifically, it is alleged that claim 15 is unclear as to which solution is being adjusted to a basic pH, and at what point during the method the solution’s pH is being adjusted.

Applicants respectfully submit that this ground of rejection has been rendered moot because claim 15 has been hereby canceled and, consequently, claims 16 and 17 no longer depend from claim 15. Accordingly, Applicants respectfully submit that claims 16 and 17 comply with the definiteness requirements of 35 U.S.C. §112, second paragraph, and, therefore, request that this rejection be withdrawn.

CLAIMS OBJECTION – INFORMALITIES

In the Office Action, claims 18-22 were objected to for the following informality:
at claim 18, line 6, “fourth” should be inserted before “aqueous.” Applicants have hereby amended claim 18 as suggested by the Examiner. Accordingly, Applicants submit that this objection has been obviated and request that it be withdrawn.

REJECTION UNDER OBVIOUSNESS-TYPE DOUBLE PATENTING

In the Office Action, claims 1-24 have been rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-27 of U.S. Patent No. 6,716,962. In addition, claims 1-5, 8-18 and 22-24 have been further rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-15 of U.S. Patent No. 6,511,962.

Applicants respectfully traverse these grounds of rejection. With regard to the rejection over U.S. Patent Nos. 6,716,962 and 6,511,962, Applicants submit herewith, without acquiescing to the assertion of the Office Action, a Terminal Disclaimer in which the statutory portion of the patent issuing from the instant application that exceeds the term of U.S. Patent Nos. 6,716,962 and 6,511,962 is disclaimed, which obviates the present rejections.

REJECTION UNDER DOUBLE PATENTING

In the Office Action, claims 1-5, 8-18, and 22-24 were rejected as not patentably distinct from claims 1-15 of U.S. Patent No. 6,511,962. To avoid an interference, a showing must be provided to show that the conflicting inventions were commonly owned at the time of invention.

As an initial matter, Applicants respectfully submit that the currently pending claims and claims 1-15 of the '962 patent are not identical and, therefore, the rejection for double patenting has been rendered moot.

Applicants respectfully submit that U.S. Patent No. 6,511,962 was, at the time the invention of U.S. Patent Application No. 09/948,374 was made, all owned by IntraBiotics

Pharmaceuticals, Inc. The Assignment of U.S. Patent No. 6,511,962 to IntraBiotics Pharmaceuticals, Inc. was recorded in the U.S. Patent and Trademark Office on January 12, 2001, at Reel No. 011476 and Frame No. 0937. The Assignment of instant U.S. Patent Application No. 09/948,374 to IntraBiotics Pharmaceuticals, Inc. was recorded in the U.S. Patent and Trademark Office on September 6, 2001, at Reel No. 012157 and Frame No. 0438. Subsequently, U.S. Patent No. 6,511,962, and U.S. Patent Application Nos. 09/904,352 and 09/948,374, were all acquired by Micrologix Biotech Inc. (now renamed Migenix Inc.), the current assignee of recorded on August 25, 2005 at Real No. 016662 and Frame No. 0582.

In view of the above statement, Applicants respectfully submit that sufficient evidence has been provided to establish common ownership of the above-identified patent and patent application at the time the invention of the instant application was made.

REJECTIONS UNDER 35 U.S.C. § 102(b)

(1) In the Office Action, claim 23 was rejected under 35 U.S.C. §102(b) as anticipated by U.S. Patent No. 3,639,582 (Umezawa *et al.*) or by U.S. Patent No. 4,331,594 (Hamill *et al.*).

Applicants respectfully submit that these grounds of rejection have been rendered moot because, as set forth above, claim 23 has been hereby cancelled without prejudice. Accordingly, Applicants respectfully request that these rejections be withdrawn.

(2) In the Office Action, claims 1-4 and 18-24 were rejected under 35 U.S.C. §102(b) as anticipated by U.S. Patent No. 3,126,317 (Heinemann *et al.*). In particular, it is alleged that Heinemann *et al.* disclose a method of isolating and purifying amphomycin from a broth containing calcium carbonate according to the instant invention.

Applicants respectfully traverse this ground of rejection and submit that Heinemann *et al.* fail to meet every limitation of the instant claims and, therefore, fail to anticipate the claimed invention. As recited in the pending claims, the instant invention is directed, in pertinent part for this rejection, to a method for purifying a lipopeptide antibiotic wherein the method comprises contacting an aqueous solution comprising a lipopeptide

antibiotic, a divalent cation, and a pH above the isoelectric point of said lipopeptide antibiotic with an organic solvent, wherein the lipopeptide antibiotic is a derivative of zaomycin, crystallomycin, amphomycin, aspartocin, glumamycin, daptomycin, antibiotic A1437, antibiotic A-21978C, antibiotic A-54145 or tsushimycin, and contacting the organic solvent extract of the lipopeptide antibiotic with acid. As discussed in greater detail below, Applicants respectfully submit that Heinemann *et al.* fail to teach or suggest extraction of a lipopeptide antibiotic into an organic solvent from an aqueous solution having a divalent cation, and having a pH above the isoelectric point of the lipopeptide antibiotic.

Heinemann *et al.* merely provide a method for isolating amphomycin from a fermentation broth wherein the broth is first acidified to pH 1.95 and then the lipopeptide is extracted into n-butanol (*see* Heinemann *et al.* at column 3, line 75 through column 4, line 2; and at column 9, lines 69-75). Thus, the extraction of amphomycin with butanol, as provided by Heinemann *et al.*, occurs only at acidic pH. As described in the instant specification (*see, e.g.*, specification at page 7, lines 5-10) and as is known in the art, an acidic lipopeptide antibiotic typically will not extract into an organic solvent when in a neutral or basic solution. In contrast, the instant invention allows for extraction of a lipopeptide antibiotic (into, for example, an organic solvent) from an acidic or basic aqueous solution, so long as the aqueous solution includes at least one divalent cation and a pH above the isoelectric point of the lipopeptide antibiotic.

Moreover, Heinemann *et al.* fail to teach or suggest the use of divalent cations during the extractive purification of amphomycin. Applicants respectfully disagree with the assertion in the Office Action that the extraction of amphomycin from broth using butanol provided by Heinemann *et al.* inherently takes place in the presence of calcium ions because the calcium ions are in the fermentation broth. Applicants agree that the initial broth contains calcium carbonate. However, acidification of the broth by Heinemann *et al.* essentially removes the calcium into the aqueous phase so that the amphomycin will partition into the organic phase, which is different from the method of the instant invention (*i.e.*, Heinemann *et al.* do not maintain the aqueous phase at a pH above the isoelectric point of the lipopeptide antibiotic; *see*,

e.g., the instant specification at page 7, line 25 through page 8, line 2). Therefore, Applicants submit that Heinemann *et al.* fail to provide every element of the instant claims.

Accordingly, Applicants respectfully submit that the instant claims distinguish patentably over Heinemann *et al.* and, therefore, satisfy the requirements of 35 U.S.C. §102(b). Applicants request that this rejection be withdrawn.

REJECTIONS UNDER 35 U.S.C. § 102(e)

In the Office Action, claims 1-4, 8, 10-13, and 16-24 was rejected under 35 U.S.C. §102(e) as anticipated by U.S. Patent No. 6,511,962.

As an initial matter, Applicants wish to note that this rejection has been rendered for claims 2-4, 10-13 and 23 since these claims have been deleted. Applicants respectfully submit that in view of the claim amendments, the rejection under 35 U.S.C. §102(e) has been rendered moot. Accordingly, Applicants respectfully request that this rejection be withdrawn.

REJECTIONS UNDER 35 U.S.C. § 103(a)

(1) In the Office Action, claims 9 and 14-17 were rejected under 35 U.S.C. §103(a) as obvious over U.S. Patent No. 6,511,962.

Applicants respectfully traverse this ground of rejection and submit that this rejection is inappropriate. In particular, common ownership has been established as set forth above. Therefore, U.S. Patent No. 6,511,962 is not available as prior art under 35 U.S.C. §103(a) as provided by 35 U.S.C. §103(c). Accordingly, Applicants request that this rejection be withdrawn.

(2) In the Office Action, claims 10 and 12 were rejected under 35 U.S.C. §103(a) as obvious over U.S. Patent No. 3,126,317 (Heinemann *et al.*). In particular,, it is asserted that it would have been obvious for one of ordinary skill in the art at the time of the instant invention to determine all operable and optimal temperatures for the different steps in the purification method of Heinemann et al. because temperature is an art-recognized,

result-effective variable that is routinely determined and optimized in the chemical and extraction arts.

Applicants respectfully traverse this ground of rejection and submit that Heinemann et al. fail to teach or suggest the claimed invention and, further, would not have motivated a person having ordinary skill in the art to arrive at the claimed invention with a reasonable expectation of success. As set forth above, Heinemann *et al.* fail to teach or suggest a method for purifying a lipopeptide antibiotic or derivative thereof according to the instant invention. In particular, Heinemann *et al.* fail to teach or suggest extraction of a lipopeptide antibiotic from an aqueous solution having a divalent cation and a pH above the isoelectric point of the lipopeptide antibiotic. Indeed, Heinemann *et al.* teach away from the extraction of a lipopeptide antibiotic from, for example, a neutral or basic aqueous solution into an organic solvent because Heinemann et al. acidify the broth containing amphotycin before extraction. Such a step would make the instant invention inoperable for its intended purpose. Moreover, a surprising result of the instant invention is the efficient extraction of lipopeptide antibiotics in general, organic solvent extraction at different pHs (not only acidic, but also at neutral and basic pH), and a dramatic increase in yield and purity without the need for additional purification such as by chromatographic methods.

Hence, Applicants respectfully submit that the Office Action has not set forth a prima facie case of obviousness, as the cited reference fails to teach every limitation of the instant invention and fails to provide motivation for a person having ordinary skill in the art to modify the prior art teachings to arrive at the claimed invention with a reasonable expectation of success. Accordingly, Applicants respectfully submit that the instant claims distinguish patentably over Heinemann et al. and, therefore, satisfy the requirements of 35 U.S.C. § 103(a). Applicants request that this rejection be withdrawn.

The Commissioner is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

All of the claims pending in the application are now believed to be allowable. Favorable consideration and a Notice of Allowance are earnestly solicited. The Examiner is urged to contact the undersigned attorney if there are any questions prior to allowance of this matter.

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Respectfully submitted,

By Jeffrey C. Pepe
Jeffrey C. Pepe, Ph.D.
Registration No.: 46,985

DARBY & DARBY P.C.
P.O. Box 5257
New York, New York 10150-5257
(206) 262-8900
(212) 527-7701 (Fax)
Attorneys/Agents For Applicant